PUBLIC ASSESSMENT SUMMARY REPORT

Pneumococcal Conjugate Vaccine, (adsorbed, 10-valent), Serum Institute of India Pvt. Ltd

What is Pneumococcal Conjugate Vaccine, (adsorbed, 10-valent)?

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) is a sterile suspension of saccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F and 23F individually conjugated by using 1-cyano-4-dimethylamino pyridinium tetrafluoroborate chemistry (CDAP) to non-toxic diphtheria CRM197 protein. The polysaccharides are chemically activated and then covalently linked to the protein carrier CRM197 to form the glycoconjugate. Individual conjugates are compounded and then polysorbate 20 and aluminium phosphate are added to formulate the vaccine. The potency of the vaccine is determined by the quantity of the saccharide antigens and the saccharide-to-protein ratios in the individual glycoconjugates. The vaccine meets the requirements of WHO, IP and BP when tested by the methods outlined in WHO TRS 977, IP and BP.

Pneumococcal Polysaccharide Conjugate Vaccine (adsorbed, 10-Valent) (PCV 10V) is a sterile homogenous suspension, presented in single dose vial 1 (0.5 mL) and 5 (2.5 mL) dose vial presentations.

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) 0.5 mL per dose contains the following:

Components	Quantity (per 0.5 mL)
Saccharide for serotypes 1, 5, 9V, 14, 19A, 19F, 23F, 7F, 6A	2 mcg each
Saccharide for serotype 6B	4 mcg
Conjugated to CRM197 carrier protein	
Aluminium (as Aluminium phosphate)	0.125 mg
*Thiomersal	0.005%

*component of the 2.5 mL multidose presentation

This liquid / ready to use vaccine is presented in USP type I transparent glass vials, stoppered with 13 mm grey rubber stopper and sealed with 13 mm aluminum flip-off plastic cap (Burgundy).

What is Pneumococcal Conjugate Vaccine, (adsorbed, 10-valent) used for?

The vaccine is used for active immunization against invasive disease, pneumonia and acute otitis media caused by *Streptococcus pneumoniae* serotypes 1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F and 23F in infants and toddlers from 6 weeks up to 2 years of age.

The use of vaccine should be determined on the basis of relevant recommendations and take into consideration the disease impact by age and regional epidemiology.

How is Pneumococcal Conjugate Vaccine, (adsorbed, 10-valent) used?

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) is to be administered as a three-dose primary series at 6, 10, and 14 weeks of age or 2, 3 and 4 months of age or 2, 4 and 6 months of age, with or without, depending on recommended dosing schedule, a booster dose at 9-10 or 12-15 months of age. The minimum interval between doses should be 4 weeks. If a booster dose is given, it should be at least 6 months after the last primary dose.

The dose is 0.5 ml given intramuscularly, with care to avoid Injection into or near nerves and blood vessels. The vaccine should be given by intramuscular injection. The preferred sites are anterolateral aspect of the thigh in infants or the deltoid muscle of the upper arm in young children. The vaccine should not be injected in the gluteal area. Do not administer Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) intravascularly. The vaccine should not be injected intradermally, subcutaneously or intravenously, since the safety and immunogenicity of these routes have not been evaluated. Once opened, multi-dose vials should be kept between +2ºC and +8ºC. Multi-dose vials of Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days, provided that all of the following conditions are met (as described in the WHO policy statement: Handling of multi dose vaccine vials after opening, WHO/IVB/14.07).

The vaccine is not to be mixed with other vaccines/products in the same syringe.

What are Pneumococcal Conjugate Vaccine, (adsorbed, 10-valent) storage characteristics?

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (10-valent) should be stored at 2 - 8º C. DO NOT FREEZE. Discard if the vaccine has been frozen.

Multi-dose Presentation: Vaccine cold chain volume per dose: 3.515 cm3/dose in secondary packaging.

Single dose Presentation: Vaccine cold chain volume per dose: 14.06 cm3/dose in secondary packaging.

Who is the regulatory authority responsible for its oversight vis a vis WHO?

The Central Drugs Standard Control Organization of India is the authority responsible for the continuing oversight of this WHO prequalified vaccine.

How has Pneumococcal Conjugate Vaccine, (adsorbed, 10-valent) been studied from the clinical point of view?

Clinical data presented by SIIPL include data from four clinical trials:
- A phase 1 trial PCV-10-001 entitled “A prospective, randomized, two-arm, active controlled, double-blind study to evaluate the safety and tolerability of Serum Institute of India’s 10-valent Pneumococcal Conjugate Vaccine (SIILPCV10) in healthy Indian young adults. *Clinical trials Registry in India: CTRI/2013/09/003961*

- A phase 1/2 study (VAC-017) entitled "A Phase 1/2, prospective, randomized, double-blind, age de-escalation study to evaluate the safety, tolerability, and immunogenicity of a 10-valent Pneumococcal Conjugate vaccine in Healthy young adults, toddlers, and infants. *Clinicaltrials.gov: NCT02308540*

- A phase 2 study (PCV-10-002) entitled "A prospective, multi-center, randomized, two arm, active controlled, double-blind study to evaluate the safety, tolerability and immunogenicity of Serum Institute of India's 10-valent Pneumococcal Conjugate Vaccine (SIILPCV10) in healthy Indian PCV- naïve toddlers (aged 12 to 15 months).
Clinical trials Registry in India: CTRI/2015/12/006456

- A phase 3 study (VAC-056) entitled "A Phase 3, randomized, double-blind study of the safety, tolerability, lot-to-lot consistency, immunogenicity and non-interference with concomitant vaccinations of Serum Institute of India's 10-valent pneumococcal conjugate vaccine (SIILPCV10) in healthy infants in The Gambia" *Clinicaltrials.gov: NCT 03197376.*

A total of 1750 people received the vaccine, including1603 young infants (6-8week old) and 113 toddlers (12-15month old) who represent the target population. The clinical trials included in the clinical development of the vaccine were conducted between 2014 and 2018 in India and the Gambia.

The vaccine demonstrated non inferiority in antibody response in comparison with all WHO prequalified PCV used as active comparators. PCV10 is also able to boost adequate antibody level when given after a primiary series.

The safety and reactogenicity profile of the vaccine was shown to be acceptable and similar to that of the two licensed and prequalified PCVs which were used as active control in this clinical program. There were no differences in the frequency, severity and nature of solicited AEs within one week of vaccination between PCV10 and the comparator vaccines. Most reactions were mild to moderate, resolving within 48 hours and in line with what can be expected following routine vaccination of infants.

Altogether the clinical findings indicate that PCV10 can safely and effectively be administered concomitantly with diphtheria, tetanus, whole-cell pertussis, Haemophilus influenzae type b, inactivated or oral poliomyelitis, rotavirus, hepatitis B, measles and rubella and yellow fever vaccines. No explanation was given for the low responses of rota virus vaccine in both groups.

Other information about evaluation of Pneumococcal Conjugate Vaccine, (adsorbed, 10-valent)

As part of the prequalification process for Pneumococcal Conjugate Vaccine, (adsorbed, 10-valent), the Common Technical Document and the responses provided by the manufacturer to observations made by WHO have been reviewed for quality, safety and efficacy by a team of WHO experts.

The dossier was prequalified following approval by Central Drugs Standard Control Organization of India.

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